

REMARKS

Claims 22, 39, and 54 have been amended in accordance with the Examiner's suggestions. Claims 6, 12, 15, 19, 24, 32, and 41 have been amended to correct a typographical error. The amendments are fully supported by the original claims and the specification and do not contain new matter. Claims 51 and 54-56 have been withdrawn by the Examiner as non-elected. In order to retain the right of rejoinder in accordance with MPEP §821.04, the Applicants have amended Claim 54 (a process of using claim) to depend on claim 1 as suggested by the Examiner. Accordingly, the Applicants note that all the withdrawn claims now depend on the compound claims or otherwise include all the limitations of the compound claims. Thus, the Applicants respectfully request rejoinder of claims 51 and 54-56 if the compound claims are deemed allowable.

The Applicants expressly rebut any presumption that the Applicants have surrendered any equivalents under the doctrine of equivalents and expressly state that the claims, as amended, are intended to include and encompass the full scope of any equivalents as if the claims had been originally filed and not amended.

Claim Rejections Under 35 USC § 112, 2nd Paragraph

Claims 22 and 39 have been rejected under 35 USC §112, second paragraph. According to the Examiner, the term "Thecompound" in claim 22 needs to be corrected and the term "characterized by" in claim 39 needs to be replaced with the term "of."

In response, the Applicants note that the claims have been amended to correct the typographical error in claim 22 and to replace the term "characterized by" with the term "of" in claim 39. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

Claim Rejections Under 35 USC § 103

Claims 1-12, 16-20, 22-26, 29-35, 39-44, 46, 47, 50, 52, and 53 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 91/19702 ("Hulin"), taken alone or in combination with WO 02/16331 (Brooks). According to the Examiner, Hulin teaches oxazole compounds that are structurally similar to the claimed compounds. The Examiner cites example 13 and formula II of Hulin wherein Z is alkyl, Z¹ is alkyl, X is O, Y is N, m is 2, W is O, ---- represents no bond, X¹ is O, R is alkyl, and Y¹ is hydroxyl. Additionally, the Examiner cites Brooks as a secondary reference and alleges that it teaches the interchangeability of hydrogen with an alkyl group on the phenyl ring of formula II in Hulin. The Applicants respectfully traverse this rejection for the following reasons.

The Applicants respectfully submit that a *prima facie* case of obviousness has not been established because there is absolutely no motivation to modify Hulin to obtain the compounds of the present invention. "To establish a *prima facie* case of obviousness . . . there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference." MPEP § 2143.01, entitled "Basic Requirements of a *Prima Facie* Case of Obviousness."

There is no motivation to modify Hulin to obtain the compounds of the present invention because: (1) all the generic structures and species in Hulin (and Brooks) are extremely broad and/or different from the presently claimed invention; and (2) the utilities or properties of the compounds disclosed in Hulin and the claimed invention are different and there is no motivation to combine Hulin with Brooks.

Teachings of Structural Similarity

The genera and species disclosed in Hulin are structurally different than the genera and species recited in the pending claims of the present application. For example, formula I in Hulin is completely different in that group A (selected from various aromatic bicyclic rings) replaces the $-(CH_2)_n-O$ group of the claimed compounds. Furthermore, the claimed compounds of the present application only relate to oxazole derivatives. In contrast, 1/12 or 8.3% of the compounds encompassed by the genus of formula II of Hulin relate to oxazoles (C_3H_3ON), since Y can be either CH or N, and X can be either S, O, NR^2 , $-CH=CH-$, $-CH=N$, or $-N=CH$. Moreover, all the generic formulations and species disclosed by Hulin are completely different from the compounds of the present invention in that the compounds of the present invention require the central phenyl moiety to be substituted. In contrast, the central phenyl moiety disclosed in Hulin is always unsubstituted.

Furthermore, the range of possible species for R, X, X^1 , Y, Y^1 , Z, Z^1 , and W in formula II of Hulin are much different and/or are extremely broad compared to the corresponding species of formula I of the claimed invention. For example, the X and Y in the five membered ring of Hulin can be S, O, NR^2 , $-CH=CH-$, $-CH=N-$, and $-N=CH-$ (for the X) and N or CH (for the Y) in contrast to the N and O in the oxazole ring of the present invention. Similarly, the Z genus in Hulin can be hydrogen, amino, (C_1-C_7)alkyl, (C_3-C_7)cycloalkyl, phenyl, or phenyl mono- or disubstituted with (C_1-C_3)alkyl, trifluoromethyl, (C_1-C_3)alkoxy, phenyl, phenoxy, benzyl, benzyloxy, fluoro or chloro. In contrast, the corresponding R^1 genus of the presently claimed invention is limited to alkyl, fluoro-lower-alkyl, cycloalkyl, bicyclic cycloalkyl, or tricyclic cycloalkyl.

In addition, the Y^1 genus in Hulin can be hydroxyl, (C_1-C_3)alkoxy, phenoxy, benzyloxy, amino, (C_1-C_4)alkanoylamino, (C_1-C_4)alkanesulfonylamino, benzenesulfonylamino, napthalenesulfonylamino, di[(C_1-C_3) alkyl]aminosulfonylamino, or one of said groups mono- or disubstituted with (C_1-C_3)alkyl, trifluoromethyl, hydroxyl,

(C1-C3)alkoxy, fluoro or chloro. In contrast, the group corresponding to Y¹ in the presently claimed invention is limited to COO-R⁸ wherein R⁸ is either hydrogen or lower-alkyl.

Moreover, the substitution pattern of the five membered cyclic ring in formula II of Hulin is extremely broad encompassing all substitution patterns for the attachment of Z and Z¹ to the ring and for the attachment of the ring to the compound. In contrast, the substitution pattern of the oxazole ring of the present invention is very specific in that R¹ is attached to the carbon between the N and O, R² is attached to the carbon adjacent to the O, and the ring itself is attached to the compound via the carbon on the ring adjacent to the N (see pending claim 1).

Similarly, Brooks discloses very broad and different generic structures and species compared to the claimed invention and provides no motivation to modify Hulin (e.g., the R³ substituent in formula I of Brooks [selected from alkyl or haloalkyl] does not exist in the generic structures or species claimed in the present application.

According to MPEP § 2144.08(4)(a), if the size of the prior art genus is broad compared to the claimed genus, one of ordinary skill in the art is less likely to be motivated to select the claimed genus or species. A rejection for obviousness is not appropriate "where the prior art does not disclose a small recognizable class of compounds with common properties." MPEP § 2144.08(II)(A)(4)(a), third paragraph, *citing In re Ruschig*, 343 F.2d 965 974 (CCPA 1965). See also *In re Deul*, 51 F.3d 1552, 1558-59 (Fed. Cir. 1995) ("[n]o particular one of these DNAs can be obvious unless there is something in the prior art to lead to the particular DNA and indicate that it should be prepared") and MPEP § 2144.09, *citing In re Langer*, 465 F2d 896 (CCPA 1972) (claims to a polymerization process using a sterically hindered amine were held unobvious over a similar prior art process because the prior art disclosed a larger number of unhindered amines and only one sterically hindered amine [which differed

from a claimed amine by 3 carbon atoms], and therefore the reference as a whole did not apprise the ordinary artisan of the significance of hindered amines as a class.).

Similarly, if the exemplified genera or species in a prior art reference are different in structure or function from what is claimed, then this “weigh[s] against selecting the claimed species or subgenus and thus against a determination of obviousness.” MPEP § 2144.08(II)(A)(4)(c), fourth paragraph. See also MPEP § 2144.08(II)(A)(4)(c), citing *In re James*, 958 F.2d 347, 350 (Fed. Cir. 1992) (reversing obviousness rejection of novel dicamba salt with acyclic structure over broad prior art genus encompassing claimed salt, where disclosed examples of genus were dissimilar in structure, lacking an ether linkage or being cyclic); *Ex parte Burtner*, 121 USPQ 345, 347 (Bd. of App. 1951) (holding claimed alcohols patentable over prior art compounds differing by a –CH₂- group).

Thus, because all the generic structures and species in Hulin (and Brooks) are extremely broad and/or different from the presently claimed invention, there is no motivation to modify Hulin (alone or in combination with Brooks) to obtain the compounds of the present invention.

Teachings of Similar Properties or Uses

There are no teachings of similar properties or uses in Hulin and the presently claimed invention; and there is no motivation to combine Brooks with Hulin. For example, the compounds disclosed in the present invention bind to and activate the peroxisome proliferator activated receptors PPAR-alpha and PPAR-gamma. In contrast, there is no indication that the compounds disclosed in Hulin bind to or activate any peroxisome proliferator activated receptor. Thus, one skilled in the art looking for compounds to bind to and activate the peroxisome proliferator activated receptors would not be motivated to select or modify the compounds of Hulin. Accordingly, there is no expectation in Hulin that structurally similar compounds bind to or activate any

peroxisome proliferator activated receptors. In addition, the Examiner has not presented proper evidence establishing a motivation to combine Hulin with Brooks in accordance the requirements of MPEP §2143.01 (“The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination” and the “fact that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish *prima facie* obviousness The level of skill in the art cannot be relied upon to provide the suggestion to combine references”).

Thus, because the utilities or properties of the compounds of the present invention are not disclosed in Hulin and since no proper evidence has been shown providing a motivation to combine Brooks with Hulin, the Applicants respectfully submit that there is no motivation to modify the prior art to obtain the compounds of the present invention.

In conclusion, since all the generic structures and species in Hulin (and Brooks) are extremely broad and/or different from the presently claimed invention, it is respectfully submitted that there is no motivation to select or obtain the presently claimed compounds from Hulin or Brooks. Furthermore, as a separate and independent reason of why there is no motivation to modify the prior art, there is no indication that the compounds disclosed in Hulin bind to or activate peroxisome proliferator activated receptors. Moreover, no evidence has been presented in accordance with MPEP §2143.01 establishing a proper motivation to combine Hulin and Brooks. Thus, for all of the above reasons, the Applicants respectfully submit that a *prima facie* case of obviousness has not been established. Accordingly, the Applicants respectfully request that the rejection under 35 U.S.C. § 103 be withdrawn.

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Entry of the foregoing remarks and amendments is respectfully requested. No fee is believed to be due in connection with the filing of this Amendment. However, if any fee is deemed necessary, authorization is given to charge the amount of any such fee to Deposit Account No. 08-2525.

Respectfully submitted,



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